Predictions??

From HIM??
He Can’t Even See Straight!
Maybe it’s not so tough after all!
Paradigm Shifting?

- Be Aware of Time Sensitivity of Applied Rx
  - Muscle Relaxants (Paralytics)
  - Proning
- Yield Ventilation Control to Patient (?)
- Reduce Demands
- Revise Therapeutic Targets
  - Monitor the key variables
- Adapt to Abnormal Physiology
- Adopt Self-Adjusting Modes that Match Need & Capability
- Exchange Gas Without Mechanical Ventilation
Goals of Mechanical Ventilation

• Effective Life Support
• Minimized Iatrogenesis
  – Less infection & VILI
• Less Invasiveness
  – Improved Interface
• Reduced Breathing Workload
  – Modes to Improve Comfort and Efficiency
  – *Better Co-ordinated with Natural Drive*
The Vent is Just a Pump....Right?
In the Beginning...
Microprocessor Control
Current Technology
Effective but…
Limited Synchrony
Limited Feedback
Our Standard Modes Of Ventilation

...For Thirty Plus Years!

SIMV

Pressure Support

Assist/ Control T-Piece

→ TROUBLE!
Resistance & Tissue Damage...
Secretions and Infection...
Lung Damage of Different Types...
De-synchronized Flow
And BreathTiming...
Asynchronous Switching, Cycling, & Power Matching
Who Becomes Asynchronous?

• High, Intermittent, and Variable Demands
  – Delirium
  – Anxiety
  – Pain
  – Severe Airflow Obstruction
  – Weakness

• Interface Problems
  – Tubing, sealing, nebulized drugs
Low Demand Neural Rhythm
High Demand Neural Rhythm
Flow Regulation  

Pressure Regulation  

Physician-Specified Values
Important Modifications For Pressure Support
Ramp Slope to Target
Flow Off-Switch

...both are *Clinician* Set
PSV Allows Variable Breath Timing But Not *Match* of Neural Cycle Length or Flow Demand
Pressure Support

Switching *Synchrony*?
Dys-synchrony!

Neural Signal
Requirement Sensitivity

Variable Tube Compensation
Why is Asynchrony Important?

Physiological Disturbances
- Hemodynamics
- Pattern of Lung Expansion
  - Efficiency of gas exchange
  - Increased work of breathing
  - Inadequate Ventilation
- Discomfort
- Sleep Interference
- Need for Sedation
Invasive Ventilation

Sedation

Complications

Critical Illness
## Asynchrony Influences Outcome

<table>
<thead>
<tr>
<th></th>
<th>Asynchrony index &lt; 10% (n=47)</th>
<th>Asynchrony index ≥ 10% (n=15)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of MV</strong></td>
<td>7 (3-20)</td>
<td>25 (9-42)</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Duration MV ≥ 7d</strong></td>
<td>23 (49%)</td>
<td>13 (87%)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Tracheostomy</strong></td>
<td>2 (4%)</td>
<td>5 (33%)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>15 (32%)</td>
<td>7 (47%)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Thille AW. ICM 2006
The *Real* Cause of Asynchrony…

What, Me Worry?
Peering into the Future??
We Must Get Away From Provider Pre-Specified Cycles

Flow Regulation

What Does The Patient Really Need?

Pressure Regulation

Neural Controller Activity Is Not Predictable, Stable or Easily ‘Captured’
Open Circuitry

Airway Pressure Release
Auto-Adjusting Modes

- **Adaptive Support (Intelligent) Ventilation**
  - Adjusts Pinsp and PC-SIMV rate to meet “optimum” breathing pattern target
- **Proportional Assist Ventilation** (Proportional Pressure Support)
  - Support pressure parallels patient effort based on mechanical outputs.
- **Neurally Adjusted Ventilatory Assist**
- **Automated Weaning (SmartCare)**
Proportional Assist Amplifies Muscular Effort Assessed By Mechanical Output
NAVA Provides Flexible Response to Effort

Ultimate Goals For Ventilation

- More Efficient
- Safer
- Less Invasive
- Improved Comfort

Better Co-ordinated with Natural Drive
Invasive Ventilation

Sedation

Complications

Critical Illness
Why *Not* Use Muscle Relaxants?

• Less efficient V/Q & gas exchange?
  – Effort, PEEP, & position dependent

• Deterioration of musculature
  – Respiratory
  – Peripheral Skeletal

• Consequences of Positive Pressure
  – Potential for hemodynamic compromise
  – Impaired lymphatic drainage
Reduced Fiber Bulk With Controlled Ventilation

Levine *NEJM* 2008
Early phase of lung-protective ventilation: A place for paralytics?*

Considerable investigative effort has addressed the problem of how best to modify the ventilatory prescription so as to limit iatrogenic damage to the acutely injured lung. By comparison, relatively little attention has been directed toward modifying the factors that drive the ventilatory demand for potentially damaging tidal volumes and airway pressures. Nevertheless, there is good reason to believe that reducing metabolic and ventilatory requirements during the crucial earliest phase of acute respiratory distress syndrome (ARDS) could yield impressive benefits, not only for gas exchange and exertion relief, but also for lung protection. Total volume and frequency—the components of minute ventilation—both contribute to the injury potential when the lung approaches or exceeds the threshold of intolerable mechanical stress. Reducing the work for ventilation allows parallel reduction in one or both. Furthermore, because thoracic recoil powers expiratory flow during passive deflation, mean transmural alveolar pressure (presumably a correlate of damaging tissue stress) will also fall with reductions of the minute ventilation requirement.

During spontaneous or machine-assisted ventilation, expiratory muscles are often called on to help meet the exertion demands of hyperpnea. Even a healthy subject who performs heavy exercise or breathes against resistance or moderate positive end-expiratory pressure recruits the expiratory muscles to take up a portion of the ventilatory burden. This “work sharing” helps to minimize or prevent hyperinflation, keeps total compliance in a favorable zone of the pressure-volume relationship, and prevents the inspiratory muscles from undertaking an otherwise fatiguing load. Unfortunately, vigorous expiratory efforts also bite into the expiratory reserve and thereby reduce the end-expiratory lung volume (1). When the lung is acutely injured, such activity encourages alveolar collapse, partially negating the effect of positive end-expiratory pressure on oxy-

*See also p. 2749.

Key Words: acute respiratory distress syndrome; mechanical ventilation; ventilator-associated lung injury; noninvasive mechanical; lung-protective ventilation

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DOI: 10.1097/01.CCM.000020732.13026.23
Triggered Ventilation Helps Preserve Diaphragm Strength

Sassoon AJRCCM 2008

- Control
- AMV
- CMV

Force/CSA (N/cm²)

Stimulation Frequency (Hz)

* Significant difference
Work of Breathing Relates \textit{Exponentially} to $V_E$

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Graph showing the relationship between work of breathing and ventilation rate.}
\end{figure}

\textbf{Otis, JAP 1950}
Silencing Effort Reduces O₂ Demand & Extraction, & ↑ FRC

Relaxed

Compression

↑ Effort
Same PEEP, Same Patient, Two FRCs
Fig 1.—Oxygen saturation recorded by ear oximetry before (closed circles) and after (open circles) paralysis with pancuronium bromide. These data present every paired set of observations available for 36-hour period.
HYPERPNEA LIMITS THE LUNG VOLUME RECRUITED BY PEEP

Chandra, Marini AJRCCM 1994
Early Paralytics May Help

Papazian *NEJM* Sept 2010

**Figure 2.** Probability of Survival through Day 90, According to Study Group.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cisatracurium (N = 177)</th>
<th>Placebo (N = 162)</th>
<th>Relative Risk with Cisatracurium (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death — no. (% [95% CI])</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 28 days</td>
<td>42 (23.7 [18.1–30.5])</td>
<td>54 (33.3 [26.5–40.9])</td>
<td>0.71 (0.51–1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>In the ICU</td>
<td>52 (29.4 [23.2–36.5])</td>
<td>63 (38.9 [31.7–46.6])</td>
<td>0.76 (0.56–1.02)</td>
<td>0.06</td>
</tr>
<tr>
<td>In the hospital</td>
<td>57 (32.2 [25.8–39.4])</td>
<td>67 (41.4 [34.1–49.1])</td>
<td>0.78 (0.59–1.03)</td>
<td>0.08</td>
</tr>
<tr>
<td>No. of ventilator-free days†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From day 1 to day 28</td>
<td>10.6±9.7</td>
<td>8.5±9.4</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>From day 1 to day 90</td>
<td>53.1±35.8</td>
<td>44.6±37.5</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>No. of days without organ failure, from day 1 to day 28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cardiovascular failure</td>
<td>18.3±9.4</td>
<td>16.6±10.4</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>No coagulation abnormalities</td>
<td>22.6±8.9</td>
<td>20.5±9.9</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>No hepatic failure</td>
<td>21.3±9.6</td>
<td>19.1±10.6</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>No renal failure</td>
<td>20.5±10.1</td>
<td>18.1±11.6</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>None of the four</td>
<td>15.8±9.9</td>
<td>12.2±11.1</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>No. of days outside the ICU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From day 1 to day 28</td>
<td>6.9±8.2</td>
<td>5.7±7.8</td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td>From day 1 to day 90</td>
<td>47.7±33.5</td>
<td>39.5±35.6</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Hospital survivors admitted to other health care facilities from day 1 to day 90 — % (95% CI)</td>
<td>22.3 (15.8–30.5)</td>
<td>18.8 (12.2–27.8)</td>
<td></td>
<td>0.52</td>
</tr>
<tr>
<td>Barotrauma — no. (% [95% CI])‡</td>
<td>9 (5.1 [2.7–9.4])</td>
<td>19 (11.7 [7.6–17.6])</td>
<td>0.43 (0.20–0.93)</td>
<td>0.03</td>
</tr>
<tr>
<td>Pneumothorax — no. (% [95% CI])</td>
<td>7 (4.0 [2.0–8.0])</td>
<td>19 (11.7 [7.6–17.6])</td>
<td>0.34 (0.15–0.78)</td>
<td>0.01</td>
</tr>
<tr>
<td>MRC score — median (IQR)§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 28</td>
<td>55 (46–60)</td>
<td>55 (39–60)</td>
<td>1.07 (0.80–1.45)</td>
<td>0.49</td>
</tr>
<tr>
<td>At ICU discharge</td>
<td>55 (43–60)</td>
<td>55 (44–60)</td>
<td>0.92 (0.71–1.19)</td>
<td>0.94</td>
</tr>
<tr>
<td>Patients without ICU-acquired paresis¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By day 28 — no./total no. (% [95% CI])</td>
<td>68/96 (70.8 [61.1–79.0])</td>
<td>52/77 (67.5 [56.5–77.0])</td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>By ICU discharge — no./total no. (% [95% CI])</td>
<td>72/112 (64.3 [55.1–72.6])</td>
<td>61/89 (68.5 [58.3–77.3])</td>
<td></td>
<td>0.51</td>
</tr>
</tbody>
</table>
Reducing Oxygen Demand May Also Reduce VILI Expression

- **Ventilation Requirement**
  - Ventilation Pressures and Cycling Frequency
- **Cardiac Output**
  - Pulmonary Blood Flow
  - Microvascular Pressure Gradient
Reducing Intensity or Number of Stress Cycles Decreases VILI

Frequency and Vascular Pressure Worsen Lung Injury

Lower Minute Ventilation
‘Take Home’ Messages

- Reducing *demand* for ventilation and oxygen delivery enables safer life support.
- Paralytics enable manipulation of ventilation patterns and position to reduce iatrogenic risk.
- *Brief* use of paralytics during the most vulnerable early period is not necessarily associated with delayed neuromuscular recovery.
- Any benefit from paralytics may depend on *vigor of* spontaneous breathing and *stage of* ARDS.
Time Sensitive Interventions

- Intravenous Fluids
- Prone Positioning
- High Level PEEP
- High Frequency Oscillation
- *Muscle Relaxants?*
Time Sensitive Interventions

- Intravenous Fluids
- **Prone Positioning**
- High Level PEEP
- High Frequency Oscillation
- Muscle Relaxants
Proning Response May Take Time

Langer *Chest* 1988
Airways Drain Best in Prone Position
Prone Positioning Relieves Lung Compression by the Heart

Albert & Hubmayr, *AJRCCM* 2000
Ventilator Induced Lung Injury 
Supine vs Prone Position

A

B

Histologic Injury Score

Supine  Prone

1.0  1.5  2.0  2.5

Histologic Injury Score

Supine  Prone

0.5  1.0  1.5  2.0  2.5

Dependent  Nondependent

Red arrow indicates comparison between Supine and Prone positions.
Classify ARDS Type, Severity, & Co-Morbidities

High Severity or Obtunded?

Non-Invasive Ventilation

Adequate ABGs & Tolerance? Stable and alert?

Yes → Continue Non-Invasive Ventilation

No → Intubate and Minimize Effort

Estimate Intravascular Volume Status

Repair Volume Deficit or Excess Establish Adequate BP

Determine Recruitment Potential With Recruiting Maneuver & PEEP Trial

Adjust PEEP and Tidal Volume

Dramatic Improvement?

Yes → Proning Contraindicated?

No → Continue Non-Invasive Ventilation

Ready for Ventilator Discontinuation?

Yes → Extubate and/or Discontinue Ventilation

No → Continue Supine 15-90° Reposition Frequently

Prone Positioning for 12-20 Hours/Day

Significant Clinical Improvement?

Yes → INO, TGI, Flo-Lan

No → Marini & Gattinoni Crit Care Med 2005
Proning May Improve Mortality in Severely Ill Patients with ARDS

Sud et al., Int Care Med 2010

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Prono n/N</th>
<th>Supine n/N</th>
<th>RR 95% CI</th>
<th>Weight %</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>92/148</td>
<td>87/149</td>
<td>27.67 1.06</td>
<td>0.88 1.28</td>
<td></td>
</tr>
<tr>
<td>Gattinoni 2001</td>
<td>4/12</td>
<td>4/9</td>
<td>0.81 0.76</td>
<td>0.25 2.22</td>
<td></td>
</tr>
<tr>
<td>Beceril 2002</td>
<td>179/413</td>
<td>139/377</td>
<td>36.30 1.09</td>
<td>0.87 1.21</td>
<td></td>
</tr>
<tr>
<td>Curley 2005</td>
<td>4/51</td>
<td>4/51</td>
<td>0.83 1.00</td>
<td>0.25 0.78</td>
<td></td>
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<tr>
<td>Voggenreiter 2005</td>
<td>1/21</td>
<td>0/12</td>
<td>0.20 0.30</td>
<td>0.03 2.67</td>
<td></td>
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<tr>
<td>Manecke 2006</td>
<td>38/76</td>
<td>37/65</td>
<td>10.47 0.81</td>
<td>0.60 1.10</td>
<td></td>
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<tr>
<td>Chan 2007</td>
<td>5/11</td>
<td>6/11</td>
<td>1.13 0.83</td>
<td>0.36 1.94</td>
<td></td>
</tr>
<tr>
<td>Fernandez 2008</td>
<td>8/21</td>
<td>10/15</td>
<td>1.97 0.80</td>
<td>0.36 1.48</td>
<td></td>
</tr>
<tr>
<td>Tecco 2009</td>
<td>79/166</td>
<td>91/172</td>
<td>9.84 0.90</td>
<td>0.79 1.11</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>910</td>
<td>887</td>
<td>100.00 0.97</td>
<td>0.86 1.07</td>
<td></td>
</tr>
<tr>
<td>Total events: 410 (Prono), 401 (Supine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: P = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.61 (P = 0.54)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Position</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prono</td>
<td>28.46 1.19</td>
</tr>
<tr>
<td>Supine</td>
<td>44.32 1.07</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Position</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prono</td>
<td>17.38 0.96</td>
</tr>
<tr>
<td>Supine</td>
<td>100.00 1.07</td>
</tr>
</tbody>
</table>

Sud et al., Int Care Med 2010

<table>
<thead>
<tr>
<th>Body Position</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prono</td>
<td>27.99 0.87</td>
</tr>
<tr>
<td>Supine</td>
<td>31.20 0.90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Position</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prono</td>
<td>13.10 0.71</td>
</tr>
<tr>
<td>Supine</td>
<td>2.42 0.88</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Position</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prono</td>
<td>23.59 0.85</td>
</tr>
<tr>
<td>Supine</td>
<td>100.00 0.04</td>
</tr>
</tbody>
</table>

Favors pron | Favors supine
Do We Really Need to Ventilate?
Percutaneous Femoral Insertion of Respiratory Catheter (HC)

- An auxiliary lung in catheter form.
- Femoral Vein
- Slides Into Position
- Occupies IVC
Intravenous Respiratory Assist Catheter
Operational Features of the HC

Pulsating balloon drives blood across membranes
Arterio-Venous Gradient Drives Flow (Passive)
Who Needs a Ventilator?
Pump-Powered Veno-Venous Flow

Hemo-lung

Schematic

Prototype

Pump Regulated Blood Flow
Two Birds...One Stone?

$\text{CO}_2 > \text{O}_2$
Therapeutic Hypothermia For ARDS?
Closing the Loop…

What Should Be Monitored?
Getting Closer to The Vital Variables

• Regional lung volumes and mechanical properties
• Assessing recruitment
• Separation of lung and chest wall mechanics
• Tissue gas exchange
• Expiratory mechanics
• Inflammation
• Event monitoring
Volume-Based Capnometry

- Deadspace
  - Anatomic
  - Physiologic
- CO₂ Production
  - Metabolic Status
  - Cardiac Output
Assessing Tissue Perfusion
OPS and SDF Microscopy
An Inadequately Addressed Problem
End-Expiration

2-Hit Pathway

Extreme Stress/Strain

Tidal Forces
(Transpulmonary and Microvascular Pressures)

Moderate Stress/Strain

Rupture

Signaling

Mechano signaling via integrins, cytoskeleton, ion channels

inflammatory cascade

Cellular Infiltration and Inflammation

Marini / Gattinoni CCM 2004
Strain ≈ (VT+FRC) / FRC
Only *Part* of the Injured Lung Inflates

Superimposed Pressure

- Inflated: 0 cmH₂O
- Small Airway Collapse: 10-20 cmH₂O
- Alveolar Collapse (Reabsorption): 20-60 cmH₂O
- Consolidation

*(modified from Gattinoni)*
What is the *Size* of the Baby Lung?
Some ‘Baby Lungs’ Are Bigger Than Others!
Absolute Aerated Lung Volume
Lung Stress is Proportional to *Trans-Alveolar Pressure*

Which *Plateau* Pressure Is Safest?

…Depends on Effort *and* Chest Wall Stiffness!
Esophageal Balloon Catheter
Trans-Pulmonary Pressure
Accounts for Effort and CW Stiffness

But *Not* for Heterogeneity…
$P_{es}$ May Be Accurate at a Vulnerable Level

Zone at High Risk
Pure Ventilator-Induced Injury

'Stretch'

'Shear'
Electrical Impedance Tomography

Cross-section of the pig thorax  
Time course of the local impedance change  
Functional EIT image of the pig thorax

Frerichs et al 1998
Two Types of Information

Static

Dynamic

Structure

Function?
Ventilator-Induced Lung Injury

HOUR 0

DORSAL

RIGHT

LEFT

VENTRAL

Poorly Vented

Well Vented
HOUR 1
Another Tool for Regional Function Assessment
Automated Mapping of Sound Amplitude
Detection, Classification, Timing and Quantitating Breath Sounds

Acoustic Signature of Crackle

When in the cycle do the crackles occur?
Auscultatory Localization
Potential Utility of *Acoustic* Monitoring

- **Dynamic Events**
  - Intra-tidal recruitment
  - Pulmonary edema
  - Bronchospasm

- **Detection of Asymmetry**
  - Pneumothorax
  - Pleural effusion
Trans-Thoracic Ultrasound

Pleural Effusion and Consolidation / Edema

Lichtenstein, Chest 2010

Lung Rockets / Comet Tails
Our Environment Can Adapt *Impressively* Over Time
Be Aware of the Shifting Paradigm!

- Observe **Time Sensitivity of Rx**
  - Paralytics
  - Proning
- **Give Ventilation Control to Patient (?)**
- **Reduce Demands**
- **Revise Targets**
  - Monitor the key variables
- **Adapt** to Abnormal Physiology
- **Exchange Gas Without** Mechanical Ventilation
Don’t Miss the Boat!

Oh, crap! Was that TODAY?
Thank You